

**CLAIMS**

We claim:

- 1    1. A method for early detection of subacute, potentially catastrophic infectious illness in a premature newborn infant comprising:
  - 3    (a) continuously monitoring heart rate variability in the premature newborn infant;
  - 4    and
  - 5    (b) identifying at least one characteristic abnormality in the heart rate variability that
  - 6    is associated with the illness.
  
- 1    2. The method of claim 1, wherein the illness is sepsis.
  
- 1    3. The method of claim 2, wherein antibiotic therapy is initiated and a diagnostic work-up for the illness, comprising obtaining a blood culture from the newborn infant, is provided when the at least one characteristic abnormality is identified.
  
- 1    4. The method of claim 1, wherein the illness is necrotizing enterocolitis.
  
- 1    5. The method of claim 4, wherein a diagnostic work-up for the illness, comprising an X-ray of the newborn infant or a pathological specimen from the newborn infant, is provided when the at least one characteristic abnormality is identified.
  
- 1    6. The method of claim 1, wherein the illness is selected from the group consisting of pneumonia and meningitis.
  
- 1    7. The method of claim 1, wherein the at least one characteristic abnormality is identified from a normalized data set of RR intervals.
  
- 1    8. The method of claim 7, wherein the data set contains on the order of about  $10^3$  to  $10^4$  sequential RR intervals.

- 1    9. The method of claim 7, wherein the at least one characteristic abnormality is  
2    identified based on at least one of the third and higher moments of the data set.
  
- 1    10. The method of claim 9, wherein the at least one moment of the data set includes  
2    the skewness of the data set.
  
- 1    11. The method of claim 10, wherein the illness is selected from the group  
2    consisting of sepsis and necrotizing enterocolitis.
  
- 1    12. The method of claim 9, wherein the wherein the at least one moment of the data  
2    set includes the kurtosis of the data set.
  
- 1    13. The method of claim 12, wherein the illness is selected from the group  
2    consisting of sepsis and necrotizing enterocolitis.
  
- 1    14. The method of claim 7, wherein the at least one characteristic abnormality is  
2    identified based on at least one percentile value of the data set.
  
- 1    15. The method of claim 14, wherein the at least one percentile value is the 10th  
2    percentile value.
  
- 1    16. The method of claim 15, wherein the illness is selected from the group  
2    consisting of sepsis and necrotizing enterocolitis.
  
- 1    17. The method of claim 7, wherein the at least one characteristic abnormality is  
2    identified based on the variance, standard deviation or coefficient of variation of the  
3    data set.
  
- 1    18. The method of claim 17, wherein the illness is selected from the group  
2    consisting of sepsis and necrotizing enterocolitis.

- 1    19. The method of claim 10, further comprising a diagnostic work-up.
- 1    20. The method of claim 12, further comprising a diagnostic work-up.
- 1    21. The method of claim 15, further comprising a diagnostic work-up.
- 1    22. The method of claim 17, further comprising a diagnostic work-up.
- 1    23. The method of claim 1, wherein a diagnostic work-up is provided when the at  
2    least one characteristic abnormality is identified.
- 1    24. A method for early detection of subacute, potentially catastrophic infectious  
2    illness in a patient comprising:
  - 3    (a) continuously monitoring the patient's RR intervals;
  - 4    (b) generating a normalized data set of the RR intervals;
  - 5    (c) calculating one or more of (i) moments of the data set selected from the third and  
6    higher moments and (ii) percentile values of the data set; and
  - 7    (d) identifying an abnormal heart rate variability associated with the illness based on  
8    one or more of the moments and the percentile values.
- 1    25. The method of claim 24, wherein the moments include the third moment of the  
2    data set.
- 1    26. The method of claim 24, wherein the moments include the fourth moment of the  
2    data set.
- 1    27. The method of claim 24, wherein the percentile values include the 10th  
2    percentile value.
- 1    28. An apparatus for early detection of subacute, potentially catastrophic infectious  
2    illness in a premature newborn infant comprising:

3 (a) a monitoring device, continuously monitoring heart rate variability in the  
4 premature newborn infant; and  
5 (b) a microprocessor, identifying at least one characteristic abnormality in the heart  
6 rate variability that is associated with the illness.

1 29. The apparatus of claim 28, wherein the microprocessor performs the step of  
2 generating a normalized data set of RR intervals.

1 30. The apparatus of claim 29, wherein the microprocessor calculates one or more  
2 of the third and higher moments of the data set and identifies the characteristic  
3 abnormality based on the one or more moments.

1 31. The apparatus of claim 30, wherein the microprocessor calculates the skewness  
2 of the data set and identifies the characteristic abnormality based on the skewness.

1 32. The apparatus of claim 30, wherein the microprocessor calculates the kurtosis of  
2 the data set and identifies the characteristic abnormality based on the kurtosis.

1 33. The apparatus of claim 29, wherein the microprocessor calculates one or more  
2 percentile values of the data set and identifies the characteristic abnormality based  
3 on the one or more percentile values.

1 34. The apparatus of claim 33, wherein the microprocessor calculates the 10th  
2 percentile value of the data set and identifies the characteristic abnormality based on  
3 the 10th percentile value.

1 35. An apparatus for early detection of subacute, potentially catastrophic infectious  
2 illness in a patient comprising (1) a monitoring device, continuously monitoring the  
3 patient's RR intervals, and (2) a microprocessor, said microprocessor performing  
4 steps comprising:  
5 (a) generating a normalized data set of the RR intervals;

6           (b) calculating one or more of (i) moments of the data set selected from the  
7           third and higher moments and (ii) percentile values of the data set;  
8           (c) identifying an abnormal heart rate variability based on one or more of  
9           the moments and the percentile values.

1     36. The apparatus of claim 35, wherein the microprocessor calculates the third  
2     moment of the data set.

1     37. The apparatus of claim 35, wherein the microprocessor calculates the fourth  
2     moment of the data set.

1     38. The apparatus of claim 35, wherein the microprocessor calculates the 10th  
2     percentile of the data set.